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Evaluation of kidney biopsies in elderly patients

Murat Tuğcu[1] · Umut Kasapoğlu[2] · Gülizar Şahin[3] · Süheyla Apaydın[4] · Gülistan Gümrükçü[5]

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Abstract

Objective The renal parenchymal disease spectrum in geriatric patients is similar to that in younger patients and can be controlled by appropriate treatment. We evaluated the clinicopathological features of kidney biopsies from geriatric patients.

Materials and methods One hundred nine native kidney biopsies from older patients (> 65 years old) obtained from 2005 to 2014 were evaluated retrospectively. The specimens were inspected by the same pathologist in the same laboratory by light microscopy and immunofluorescence.

Results The mean age of the patients was 72.4 ± 7.8 years (range 65–90 years), and 51.3% were female. The most frequent indication for kidney biopsy was proteinuria at the nephrotic level (56.8%). The most frequent histopathological diagnoses were focal segmental glomerulosclerosis in primary glomerulonephritis and secondary amyloidosis in secondary glomerulonephritis. The rate of major complications due to kidney biopsy was < 1%.

Result Kidney biopsy is an effective and safe method of evaluating renal parenchymal diseases in older patients.

Keywords Geriatric · Kidney biopsy · Glomerulonephritis · Complication

Introduction

Over the last two centuries, the burden of disease has increased steadily in older patients with the prolonged life expectancy. The resulting morbidity has led to the concept of prolonged healthy life expectancy. In nephrology practice, the number of older patients is increasing [1], and measures to prevent the development of renal failure and to prolong the healthy life expectancy have gained importance in terms of both medical and financial aspects.

Formerly, given the low prevalence and poor prognosis of glomerulonephritis in older patients, diagnostic and therapeutic interventions were not prioritized [2]. However, the spectrum of renal parenchymal disease in older patients is similar to that in younger patients; only the frequency of diseases differs according to age [3]. Moreover, diagnoses made via kidney biopsy in older patients can be controlled by appropriate treatment, and complications are not more frequent in patients in this age group [4–6]. We evaluated the clinicopathological features of kidney biopsies conducted in our clinic in older patients.

✉ Murat Tuğcu
drmrttgc@hotmail.com

Umut Kasapoğlu
drciftkaplan@gmail.com

Gülizar Şahin
gulimanga@yahoo.com

Süheyla Apaydın
suheylaapaydin@yahoo.com

Gülistan Gümrükçü
gulistangumrukcu@gmail.com

1 Department of Nephrology, Marmara University Pendik Training and Research Hospital, Fevzi Çakmak Mahallesi, Muhsin Yazıcıoğlu Cd No: 10, 34899 Istanbul, Turkey

2 Department of Nephrology, Agrı Public Hospital, Agrı, Turkey

3 Department of Nephrology, Sultan Abdulhamid Han Training and Research Hospital, Istanbul, Turkey

4 Department of Nephrology, Bakirkoy Sadi Konuk Training and Research Hospital, Istanbul, Turkey

5 Department of Nephrology, Haydarpasa Numune Training and Research Hospital, Istanbul, Turkey

Materials and methods

One hundred nine native kidney biopsies obtained from older patients (> 65 years old) at Haydarpasa Numune Training and Research Hospital from 2005 to 2014 were evaluated retrospectively. Data on age, sex, kidney biopsy indications, and histopathological characteristics were obtained from the medical records. Prior to biopsy, kidney function, hemoglobin level, platelet count, prothrombin time, and active partial thromboplastin time were evaluated, and written informed consent was obtained from each patient. Among the biopsies performed using 16–18-G half-72 automatic needles accompanied by the acquisition of two core samples by ultrasound, those with fewer than seven glomeruli, transplanted kidney biopsies, those from patients aged < 65 years, and samples with insufficient clinical information were excluded. All biopsy specimens were inspected by the same pathologist in the same laboratory by light microscopy and immunofluorescence. Electron microscopic examination was not performed.

The indications for kidney biopsy were classified as: (1) acute kidney injury (AKI, defined as a sudden increase (over several days to weeks) in the serum creatinine level of ≥ 0.3 mg/dL (≥ 26.4 µmol/L) or ≥ 50% from baseline and/or a reduction in urine output of < 0.5 mL/kg/h for more than 6 h) or chronic kidney disease (CKD, defined as an elevated serum creatinine level for > 3 months and/or detection of bilateral small kidneys or a unilateral small single kidney by radiological imaging), (2) nephrotic-range proteinuria (> 3.5 g/24 h proteinuria and absence of hematuria), (3) abnormal urine findings (non-nephrotic proteinuria and hematuria), (4) isolated proteinuria (< 3.5 g/24 h and no hematuria), and (5) isolated hematuria (micro- or macrohematuria without proteinuria).

Pathological classifications were primary glomerulonephritis, secondary glomerulonephritis, tubulointerstitial diseases, vascular diseases, and other. Primary glomerulonephritis was classified as focal segmental glomerulosclerosis (FSGS), immunoglobulin A nephropathy (IgAN), membranous nephropathy (MN), minimal change disease (MCD), pauci-immune vasculitis, membranoproliferative glomerulonephritis, and other glomerulonephritis. Secondary glomerulonephritis was classified as lupus nephritis (LN), diabetic nephropathy (DN), secondary amyloidosis (AA), primary amyloidosis (AL), light chain disease (LCD), cast nephropathy (CN), and systemic vasculitis (e.g., anti–glomerular basement membrane [GBM] disease). Tubulointerstitial disease was classified as acute tubular necrosis (ATN), acute tubulointerstitial nephritis (ATIN), chronic tubulointerstitial nephritis (CTIN), and chronic pyelonephritis (CPN). Vascular diseases were classified as hypertensive nephropathy (HN) and thrombotic microangiopathy.

Table 1 Baseline characteristics of patients aged over 65 years

Male/female (*n*)	53/56
Age	72.4 ± 7.8 years
Blood creatinine	2.9 ± 2.8 mg/dL
Proteinuria	5.3 ± 4.6 gr/day
Hematuria (*n*)	46
Glomeruli number	13.7 ± 6.6 units
Hypertensive patients (*n*)	73
Diabetic patients (*n*)	32

Table 2 Kidney biopsy complications of patients in the study

Complications	*n*
Minor (localized hematomas causing pain)	4
Major (erythrocyte transfusion due to hemorrhage)	1

Data obtained from patient files and hospital records were analyzed statistically with SPSS v. 18. Continuous variables were expressed as medians (ranges) or means ± standard deviations, and categorical variables were expressed as proportions (%). Comparisons between groups were performed using the non-parametric Chi-square test. p value < 0.05 was considered to be statistically significant.

Results

One hundred nine kidney biopsies performed on patients aged ≥ 65 years in Haydarpasa Numune Training and Research Hospital from 2005 to 2014 were evaluated retrospectively. The mean age of the patients was 72.4 ± 7.8 years (range 65–90 years), and 56 (51.3%) of the patients were female. The mean serum creatinine level was 2.9 ± 2.8 mg/dL, the mean proteinuria level was 5.3 ± 4.6 g/day, and the number of glomeruli was 13.7 ± 6.6 units (Table 1). Of the five patients who developed complications, four had minor complications (localized hematomas causing pain), and one patient (< 1%) had a major complication, hemorrhage, for which they underwent erythrocyte replacement (Table 2). Among the laboratory parameters of the patients with non-specific histological findings (interstitial fibrosis, tubular atrophy, and vascular changes [arteriosclerosis and/or hyalinosis]), only the plasma creatinine level was correlated significantly with interstitial fibrosis (4.1 ± 3.9 vs. 2.6 ± 2.4, $p = 0.026$) and tubular atrophy (3.4 ± 2.9 vs. 2.1 ± 2.5, $p = 0.019$; Table 3).

The most common indication for kidney biopsy was nephrotic-range proteinuria ($n = 62$, 56.8%). In biopsies performed due to nephrotic-range proteinuria, MN ($n = 10$, 9.2%)

Table 3 Correlation between laboratory values and non-specific histological findings

	Interstitial fibrosis		Tubular atrophy		Vascular changes (Arteriosclerosis and/or hyalinosis)	
	(+)	(−)	(+)	(−)	(+)	(−)
	n: 20	*n*: 89	*n*: 67	*n*: 42	*n*: 53	*n*: 56
Plasma creatinine value (mg/dL)	4.1 ± 3.9	2.6 ± 2.4	3.4 ± 2.9	2.1 ± 2.5	3.1 ± 2.6	2.8 ± 2.9
	***p*: 0.026**		***p*: 0.019**		*p*: 0.634	
Proteinuria (gr/day)	5.1 ± 4.7	5.4 ± 4.7	4.9 ± 4.5	6.1 ± 4.8	5.5 ± 4.2	5.2 ± 5.1
	p: 0.767		*p*: 0.199		*p*: 0.743	

Bold values indicate that plasma creatinine level was correlated significantly with interstitial fibrosis and tubular atrophy

was the most frequent primary glomerulonephritis, and AA ($n=18$, 16.5%) was the most frequent secondary glomerulonephritis. Renal failure was the second most frequent indication for renal biopsy. Biopsies performed for renal failure were divided into AKI ($n=20$) and CKD ($n=20$) subgroups. Acute tubulointerstitial diseases ($n=5$, 4.6%) and pauci-immune vasculitis ($n=5$, 4.6%) were the most frequent findings in biopsies from patients with AKI; FSGS ($n=6$, 5.5%) and AA ($n=5$, 4.6%) were the most frequent findings in biopsies from patients with CKD. Other indications, in order of frequency, were isolated proteinuria ($n=4$, 3.6%), and asymptomatic urine findings ($n=3$, 2.7%; Table 4).

Secondary glomerulonephritis was the most common renal disease ($n=44$, 40.3%). The rates of primary glomerulonephritis, tubulointerstitial disease, unidentified renal parenchymal disease, and vascular diseases were 36.7%, 12.8%, 6.4%, and 3.6%, respectively (Table 5).

Among patients with secondary glomerulonephritis, the rates of the most common pathological diagnoses were: AA 22.9%, DN 7.3%, AL/LCD/CN 5.5%, LN 3.6%, and anti-GBM disease 0.9%. Secondary amyloidosis was caused by familial Mediterranean fever (FMF; $n=6$), tuberculosis ($n=4$), rheumatoid arthritis (RA; $n=4$), bronchiectasis ($n=3$), and other (lymphoma, Crohn's disease, chronic osteomyelitis, and idiopathic; $n=8$). DN was the second most common secondary glomerulonephritis ($n=8$). The majority of patients diagnosed with DN ($n=7$) were biopsied due to nephrotic-range proteinuria. The rates of the most common types of primary glomerulonephritis were: FSGS 13.8%, MN 10.1%, pauci-immune vasculitis 5.5%, IgAN 3.6%, and MCD 3.6% (Table 5). The most of the patients diagnosed with FSGS ($n=9$) were biopsied due to nephrotic-range proteinuria.

Discussion

The functional and structural changes in the kidney that occur due to aging and the high prevalence of hypertension and diabetes in older patients result in a complex clinical picture. In addition, the co-existence of several renal parenchymal diseases is more common in older patients [7, 8]. For these reasons, accurate diagnosis in older patients without kidney biopsy can be difficult. An increasing amount of information about the pattern of biopsy-proven kidney diseases in adult patients aged > 65 years is available. We analyzed clinical and pathological data from 109 geriatric patients, and kidney biopsy was safe and successful in providing a definitive diagnoses.

In several studies, the most common indication for renal biopsy in geriatric patients was nephrotic-range proteinuria, similar to our study [3, 4, 8–10]. And also, two studies conducted in Turkey yielded same results [11, 12]. In biopsies performed due to nephrotic-range proteinuria, diagnosis of MN was found most frequently among primary glomerulonephritis, and that of AA was detected most frequently among secondary glomerulonephritis. In our study, AKI and CKD were two important kidney biopsy indications after nephrotic-range proteinuria. Similarly, in a study conducted in Italy, CKD was the second most common indication for biopsy, after nephrotic syndrome, in older patients [9]; in a study conducted in Spain, AKI was the second most important indication for renal biopsy, after nephrotic syndrome [10]. Furthermore, in two studies conducted in very elderly patients, AKI was the most common indication for kidney biopsy [13, 14].

Unsurprisingly, pauci-immune vasculitis is reportedly the most common diagnosis in biopsies performed for AKI [3, 4, 9, 13], similar to our study, likely because of the high prevalence of this condition in older patients [15]. In our study, ATN and ATIN was the second and third most common diagnoses after pauci-immune vasculitis. Although diagnosis of ATN and ATIN may be clinically established in most of patients, in some cases biopsy is needed. The increasing incidence of ATN and ATIN in older patients may be attributed to age-related anatomical changes in the kidney and various renal stressors, such as use of multiple medicines, exposure to contrast media, obstructive uropathy, frequent invasive procedures, and greater sensitivity to infections

Table 4 Correlation between biopsy indication and histological findings

Biopsy indications	Histological diagnosis	Number of patients	Ratio (%)
Nephrotic-range proteinuria	AA	18	16.5
	MN	10	9.2
	FSGS[a]	9	8.3
	DN	7	6.4
	MCD	4	3.6
	IgAN	3	2.7
	HN	2	1.8
	Non-diagnostic	2	1.8
	LN	1	0.9
	AL	1	0.9
	CN	1	0.9
	Pauci-immune vasculitis	1	0.9
	CPN	1	0.9
	LCD	1	0.9
Acute renal failure	Pauci-immune vasculitis	5	4.6
	ATN	5	4.6
	ATIN	2	1.8
	MN	1	0.9
	LN	1	0.9
	CN	1	0.9
	LCD	1	0.9
	SSRC	1	0.9
	Anti-GBM	1	0.9
Chronic renal failure	FSGS[a]	6	5.5
	AA	5	4.6
	Non-diagnostic	4	3.6
	CPN	3	2.7
	CTIN	2	1.8
	DN	1	0.9
	IgAN	1	0.9
	HN	1	0.9
Isolated proteinuria	AA	2	1.8
	AL	1	0.9
	Non-diagnostic	1	0.9
Abnormal urine findings	LN	2	1.8
	CPN	1	0.9
Total		109	100

FSGS Focal segmental glomerulosclerosis, *IgAN* IgA nephropathy, *MN* Membranous nephropathy, *MCD* Minimal change disease, *MPGN* Membranoproliferative glomerulonephritis, *LN* Lupus nephritis, *DN* Diabetic nephropathy, *AA* Secondary amyloidosis, *AL* Primary amyloidosis, *LCD* Light chain disease, *CN* Cast nephropathy, *Anti-GBM* Anti-glomerular basement membrane disease, *ATN* Acute tubular necrosis, *ATIN* Acute tubulointerstitial nephritis, *CTIN* Chronic tubulointerstitial nephritis, *CPN* Chronic pyelonephritis, *HN* Hypertensive nephropathy, *SSRC* Systemic sclerosis renal crisis

[a] It was not possible to differentiate primary and secondary FSGS. Because of the indication of biopsy in FSGS cases with subnephrotic proteinuria was CKD and electron microscopy could not be used in our study

and dehydration [16]. Supporting these data, several studies yielded similar results as ours [3, 8, 9]. Furthermore, in a study, the most common diagnosis in geriatric patients with AKI is reported to be ATIN, followed by ATN [17]. In our study, the high number of biopsied patients because of CKD with unknown etiology may related to the policy of our clinic that performing biopsy whose kidneys dimension are not reduced even if patient is elderly or has high blood

Table 5 Histological diagnosis

	Number of patients	Ratio (%)
Primary glomerulonephritis	40	36.7
FSGS	15	13.8
MN	11	10.1
Pauci-immune vasculitis	6	5.5
IgAN	4	3.6
MCD	4	3.6
Secondary glomerulonephritis	44	40.4
AA	25	22.9
DN	8	7.3
AL/CN/LCD	6	5.5
LN	4	3.6
Anti-GBM	1	0.9
Tubulointerstitial nephritis	14	12.8
ATN	5	4.6
CPN	5	4.6
ATIN/CTIN	4	3.6
Vascular diseases	4	3.6
HN	3	2.7
SSRC	1	0.9
Non-diagnostic	7	6.4

FSGS Focal segmental glomerulosclerosis, *IgAN* IgA nephropathy, *MN* Membranous nephropathy, *MCD* Minimal change disease, *MPGN* Membranoproliferative glomerulonephritis, *LN* Lupus nephritis, *DN* Diabetic nephropathy, *AA* Secondary amyloidosis, *AL* Primary amyloidosis, *LCD* Light chain disease, *CN* Cast nephropathy, *Anti-GBM* Anti-glomerular basement membrane disease, *ATN* Acute tubular necrosis, *ATIN* Acute tubulointerstitial nephritis, *CTIN* Chronic tubulointerstitial nephritis, *CPN* Chronic pyelonephritis, *HN* Hypertensive nephropathy, *SSRC* Systemic sclerosis renal crisis

creatinine value and FSGS and AA were the most common diagnosis in biopsied patients with the indication of CKD. This result is probably due to the fact that FSGS and AA are the two most common glomerular diseases detected in our patients.

In several studies, MN was the most frequent primary glomerulonephritis in older patients [3, 4, 6]; this result has been confirmed in two studies conducted in Turkey, in which FSGS was the second most frequent primary glomerulonephritis [11, 12]. Similarly, in a Polish study involving 14 centers, MN and FSGS were the most frequently detected types of glomerulonephritis, respectively [18]. But, in our study, FSGS was the most common primary glomerulonephritis, followed by MN. Probably in our cases, especially those with proteinuria at the subnephrotic level, it may be secondary FSGS. However, it is not possible to conclude a definitive decision since the indication of biopsy in cases with subnephrotic proteinuria was CKD. In this case, proteinuria may not be at nephrotic level as a result of chronicity, moreover we could not use electron microscopy examination in our study. Nevertheless, the incidence of FSGS has increased worldwide [19, 20], possibly due to an increased awareness of FSGS or to an increased incidence of FSGS in older patients secondary to diseases such as hypertension and age-related nephropathy [13].

Moutzouris et al. [13] reported that the most common secondary glomerulonephritis is AA; this result was replicated in two Turkish studies [11, 12] and our study revealed similar results. This high number of AA in our study and country might be attributed to FMF is an endemic disease and the most common cause of AA in Turkey [21] and also the incidence of AA reportedly increases with age [22]. Interestingly, DN was the second most common secondary glomerulonephritis in this study. Also, Jin et al. [8] reported that DN was the most common secondary glomerulonephritis in geriatric patients. The higher frequency of DN in our study might be due to our biopsy decision is more liberal and we tend to biopsy in elderly diabetic patients especially with nephrotic-range proteinuria regardless of diabetic retinopathy and other urinary abnormalities. Because independent of biopsy indication and evaluation using only clinical data could lead to misinterpretation of diabetic nephropathy, and the gold standard for diagnosis is kidney biopsy [23, 24].

The incidence of major complications was $< 1\%$, that only one patient required erythrocyte replacement due to hemorrhage. And the minor complications were subcapsular hematoma with pain (Table 2). Other studies have also reported similar complication rates [25, 26].

This study has several limitations. First, it was a retrospective evaluation of related data. Second, immune parameters, such as anti-neutrophil cytoplasmic antibodies and viral serological attributes, were not evaluated. Third, the outcomes of postbiopsy treatments could not be evaluated. Fourth, we did not compare the demographic and clinicopathological factors of our patient group with those of younger patients. Therefore, our results need to be confirmed in larger and more-detailed prospective cohort studies.

Conclusion

The population of Turkey is aging [6], a trend that is projected to continue. In nephrology practice, older patients are frequently seen and have distinctive features. Furthermore, kidney biopsy in older patients is a safe and useful procedure. Then, clinicopathological assessment of kidney biopsies from older patients will facilitate the assessment of renal parenchymal diseases.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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